

REMARKS

Claims 1-19 and 22-55 are pending in the application. Claims 1-2, 4, 7-10 and 52 have been allowed. Claims 5, 33-51, 53 and 55 have been canceled without prejudice or disclaimer. Claims 3, 6, 11, 17, 19 and 22 have been amended to better clarify what Applicants regard as the invention. Support for the amendments can be found throughout the specification, but particularly on page 16, lines 8-11; on page 16, lines 21-22 continuing on to page 17, lines 1-13; and on page 23, lines 13-22 continuing on to page 24, line 1. The specification has been amended to include a Sequence Identifier (SEQ ID NO: 2) in the paragraph on page 23, lines 13-22, continuing on to page 24, line 1. In addition, a Substitute Sequence Listing has been provided in paper and computer readable format along with a Statement in support of same. No new matter has been added by way of this amendment. Thus, as a result of the foregoing amendment, claims 1-4, 6-19, 22-32, 52 and 54 are under consideration. Reconsideration of this application is respectfully requested.

Applicants' representatives would like to express their sincere appreciation for the telephonic discussion held with Examiner Wehbe on January 20, 2006 as related to the proposed claim amendments to be submitted with the response to the recent Office Action. In that conversation, Examiner Wehbe noted that the proposed claim amendments were acceptable for placing the application in condition for allowance, provided that Applicants canceled the withdrawn claim numbers 33-51 and 53. Accordingly, and on this basis, Applicants submit herewith the claims as discussed with the Examiner and have canceled the withdrawn claims without prejudice or disclaimer. Applicants reserve the right to pursue these claims in a Divisional or Continuation application.

Rejection under 35 U.S.C. §112, second paragraph

Claims 3, 5, 6, 11-19, 22-32 and 54-55 were rejected under 35 U.S.C. §112, second paragraph as being indefinite. In particular, the Examiner alleges that the claims are unclear for the following reasons:

In particular, the Examiner alleges that claim 3 recites the mammal of claim 2, "wherein a polynucleotide encoding said at least two detectable proteins present at the C-

terminus of the gene product of said fusion polynucleotide are located in exon G1". The Examiner alleges that since claim 1, upon which claim 3 ultimately depends has been amended to delete the language of a polynucleotide sequence encoding a detectable protein and now recites a "fusion polynucleotide comprising a nucleic acid encoding at least two detectable proteins," the Examiner suggests that claim 3 be amended to recite, "wherein said nucleic acid encoding said at least two detectable proteins....". Likewise, since claim 5 depends on claim 4, which depends on claim 1, the Examiner also suggests that claim 5 should be amended to recite similar language.

Applicants respectfully traverse the Examiner's rejection, but have amended claim 3 as suggested by the Examiner in order to place the application in condition for allowance. Claim 3 now recites:

"The genetically-modified non-human mammal of claim 2 wherein said nucleic acid encoding said at least two detectable proteins present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1."

Based on the foregoing amendment to claim 3, withdrawal of the rejection is respectfully requested.

The Examiner further alleges that claim 5 as amended is confusing in that it is unclear whether the flexible linker is actually encoded by the fusion polynucleotide.

Claim 5 has been canceled without prejudice or disclaimer, thus obviating the Examiner's rejection.

The Examiner further alleges that claims 6 and 22 recite the limitation "said immunoglobulin heavy chain gene" and that there is insufficient antecedent basis for this limitation in the claims.

Applicants respectfully traverse the Examiner's rejection and have amended claim 6 to recite:

"The genetically-modified non-human mammal of claim 1 wherein said immunoglobulin heavy chain is selected from the group consisting of IgG, IgM, IgD and IgA."

Furthermore, claim 22 has also been amended to recite:

“The genetically-modified immune cell of claim 17 wherein said immunoglobulin heavy chain is selected from the group consisting of IgG, IgM, IgD and IgA.”

Applicants assert that there is sufficient antecedent basis for claims 6 and 22, as currently amended. Withdrawal of the rejection is respectfully requested.

The Examiner also alleges that claim 11 recites the limitation “the polypeptide” and that there is insufficient antecedent basis for this limitation in the claim. Further, the Examiner notes that since claim 1 refers to a fusion polynucleotide, it is unclear whether the linker sequences referred to are amino acid sequences or nucleic acid sequences. Since claims 12-16, and 54 depend from claim 11, the Examiner has included these claims in this rejection.

Applicants respectfully traverse the Examiner’s rejection and have amended claim 11 to recite:

“The genetically-modified non-human mammal of claim 1 wherein at least one of the at least two detectable proteins is an autofluorescent protein, a visibly-detectable protein, an enzymatically active protein, or a protein capable of interacting with another molecule to produce a detectable product.”

Applicants assert that there is sufficient antecedent basis for claim 11, as amended, and as such, withdrawal of the rejection of claim 11, as well as of claims 12-16 and 54, which depend from claim 11, is respectfully requested.

The Examiner alleges that claim 17 is confusing in that as amended the claim recites a fusion polynucleotide comprising a nucleic acid encoding an immunoglobulin component and a nucleic acid encoding at least two detectable proteins, “wherein a flexible linker peptide is located between the immunoglobulin and the at least two detectable proteins...”. The Examiner notes that since the claim refers to a polynucleotide, it is unclear whether the applicant intends that the polynucleotide actually include a linker peptide or whether the applicant means to claim that the fusion polynucleotide further comprises a nucleic acid sequence encoding the immunoglobulin component and the nucleic acid encoding the at least two detectable proteins. Since claims 18-19, 22-32 and 54 depend on claim 17, the Examiner has included these claims

in this rejection.

Applicants respectfully traverse the Examiner's rejection and have amended claim 17 to recite:

"A genetically-modified immune cell having a single vector comprising a fusion polynucleotide, said fusion polynucleotide comprising a nucleic acid encoding an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, a nucleic acid encoding at least two detectable proteins, and a nucleic acid encoding a flexible linker peptide located between the nucleic acid encoding the immunoglobulin component and the nucleic acid encoding the at least two detectable proteins, and wherein said immune cell is capable of expressing at least two detectable proteins fused with said immunoglobulin component, with the flexible linker peptide between the immunoglobulin component and the at least two detectable proteins, wherein antibodies secreted by said genetically-modified immune cell comprise said at least two detectable proteins."

Applicants assert that the claim as amended sufficiently clarifies the genetic construct of the cell, which comprises a nucleic acid encoding an immunoglobulin component, and a nucleic acid encoding the at least two detectable proteins, with a nucleic acid encoding the flexible linker peptide therebetween. As such, withdrawal of the rejection of claim 17, as well as of claims 18-19, 22-32 and 54, which depend from claim 17, is respectfully requested.

The Examiner also alleges that claim 19 which depends on claim 17, recites "wherein a polynucleotide encoding said at least two detectable proteins present at the C-terminus of the gene product...". The Examiner notes that claim 17, upon which claim 19 depends has been amended to delete the language of a polynucleotide sequence encoding a detectable protein, and as amended claim 17 now refers to a fusion polynucleotide comprising a nucleic acid encoding at least two detectable proteins. The Examiner has suggested that claim 19 be amended to recite, "wherein said nucleic acid encoding said at least two detectable proteins...".

Applicants respectfully traverse the Examiner's rejection and have amended claim 19 as suggested in order to place the application in condition for allowance.

Claim 19 now recites:

"The genetically-modified immune cell of claim 17, wherein said nucleic acid encoding said at least two detectable proteins present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1."

The Examiner also alleges that claim 55 depends on claims 11 or 27 and recites, "wherein said detectable protein may be one of at least two detectable proteins or a plurality of detectable proteins, in tandem or not in tandem" and that the claim is confusing because the base claim upon which it depends, claims 11 or 17 respectively, refer to a fusion polynucleotide encoding at least two detectable proteins. Thus, the Examiner notes that the mammals or cells are already limited to at least two detectable proteins and therefore it is unclear how claim 55 further limits the parent claims. The Examiner also alleges that it is unclear which of the two detectable proteins "said detectable protein" is referring to.

Applicants respectfully traverse the Examiner's rejection, and have canceled claim 55 in order to place the application in condition for allowance. Withdrawal of the rejection is respectfully requested.

Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or to credit any overpayments.

Conclusion

Applicants believe that the outstanding rejections based on 35 U.S.C. §112 second paragraph have been overcome by the amendments presented above. Thus, reconsideration and withdrawal of the outstanding grounds of rejection, and early allowance of the claims as amended is believed to be in order and is courteously solicited.

In the event that there are any questions concerning this amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned at the number listed below, so that prosecution of the application may be expedited.

Respectfully submitted,

A handwritten signature in cursive script, reading "Veronica Mallon".

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Attachments: Substitute Sequence Listing in paper and computer readable form and Statement